SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ZOFENAC 50 TABLET

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains:
Diclofenac Sodium BP 50mg

Colour: Sunset Yellow FCF

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short-term treatment of all grades of pain and inflammation in the following acute conditions:

- Posttraumatic pain, inflammation and swelling, e.g. due to sprains.
- Acute musculo-skeletal disorders such as periarthritis (for example frozen shoulder), tendonitis, tenosynovitis, bursitis.
- Post operative pain, inflammation and swelling, e.g. following dental or orthopaedic surgery.
- Painful and/or inflammatory conditions in gynaecology, e.g. primary dysmenorrhoea or adnexitis and associated menorrhagia.
- Migraine attacks.
- Acute gout
- Painful syndromes of the vertebral column.
- Non-articular rheumatism.
- As an adjuvant in severe painful inflammatory infections of the ear, nose or throat, e.g. pharyngotonsillitis, otitis. In keeping with general therapeutic principles, the underlying disease should be treated with basic therapy, as appropriate. Fever alone is not an indication.

4.2 Posology and method of administration

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms .The tablets should be

swallowed whole with liquid, preferably before meals, and must not be divided or chewed. Adults The recommended initial daily dose is 100 to 150 mg. In milder cases, 75 to 100 mg daily is usually sufficient. The total daily dose should generally be divided in 2 to 3 doses. In primary dysmenorrhoea, the daily dose should be individually adjusted and is generally 50 to 150 mg. A dose of 50 to 100 mg should be given initially and, if necessary, increased over the course of several menstrual cycles up to a maximum of 200 mg/day. Treatment should be started on appearance of the first symptoms and, depending on the symptomatology, continued for a few days.

In migraine, an initial dose of 50 mg should be taken at the first signs of an impending attack. In cases where pain relief within 2 hours after the first dose is not sufficient, a further dose of 50 mg may be taken. If needed, further doses of 50 mg may be taken at intervals of 4 to 6 hours, not exceeding a total dose of 200 mg per day. Children and adolescents: ZOFENAC 50 tablets are not recommended for use in children and adolescents below 14 years of age; other forms of diclofenac such as oral drops or suppositories could be used in these patients. For adolescents aged 14 years and over, a daily dose of 75 to 100 mg is usually sufficient. The total daily dose should generally be divided in 2 to 3 doses. The maximum daily dose of 150 mg should not be exceeded. The use of ZOFENAC 50 (all forms) in migraine attacks has not been established in children and adolescents. Older people (Patients aged 65 or above) Although the pharmacokinetics of ZOFENAC 50 are not impaired to any clinically relevant extent in elderly patients, non-steroidal anti-inflammatory drugs should be used with particular caution in frail elderly patients or those with a low body weight. In particular, it is recommended that the lowest effective dosage be used in these patients

4.3 Contraindications

- Known hypersensitivity to the active substance or to any of the excipients.
- Active gastric or intestinal ulcer, bleeding or perforation
- History of gastrointestinal bleeding or perforation, related to previous NSAIDs therapy. Active or history of recurrent peptic ulcer/ haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- Last trimester of pregnancy (see section 4.6 Pregnancy and lactation).
- Hepatic failure
- Chronic Kidney Disease Grade 5

4.4 Special warnings and precautions for use

General Undesirable effects may be minimised by using the lowest effective dose for the shortest possible duration necessary to control symptoms .The use of ZOFENAC 50 with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors, should be avoided due to the absence of any evidence demonstrating synergistic benefits and the potential for additive undesirable effects. Caution is indicated in the elderly on basic medical grounds especially used in frail elderly patients or those with a low body weight. Like other NSAIDs, ZOFENAC 50 may mask the signs and symptoms of infection due to its pharmacodynamic properties.

4.5 Interaction with other medicinal products and other forms of interaction

The following interactions include those observed with ZOFENAC 50 sugar-coated tablets and/or other pharmaceutical forms of diclofenac. CYP2C9 inhibitors: Caution is recommended when co-prescribing diclofenac with CYP2C9 inhibitors (such as voriconazole), which could result in a significant increase in peak plasma concentrations and exposure to diclofenac. CYP2C9 inducers: Caution is recommended when co-prescribing diclofenac with CYP2C9 inducers (such as rifampicin), which could result in a significant decrease in plasma concentration and exposure to diclofenac.

Lithium: If used concomitantly, diclofenac may raise plasma concentrations of lithium. Monitoring of the serum lithium level is recommended.

Digoxin: If used concomitantly, diclofenac may raise plasma concentrations of digoxin. Monitoring of the serum digoxin level is recommended. Diuretics and antihypertensive agents: Like other NSAIDs, concomitant use of diclofenac with diuretics or antihypertensive agents (e.g. beta-blockers, angiotensin converting enzyme (ACE) inhibitors) may cause a decrease in their antihypertensive effect. Therefore, the combination should be administered with caution and patients, especially the elderly, should have their blood pressure periodically monitored. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter, particularly for diuretics and ACE inhibitors due to the increased risk of nephrotoxicity

4.6 Fertility, pregnancy, and lactation

Pregnancy- Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo/foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac malformation and gastroschisis after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1%, up to approximately 1.5 %.

Lactation Like other NSAIDs, diclofenac passes into the breast milk in small amounts. Therefore, ZOFENAC 50 should not be administered during breast feeding in order to avoid undesirable effects in the infant.
Fertility As with other NSAIDs, the use of ZOFENAC 50 may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of ZOFENAC 50 should be considered.

4.7 Effects on ability to drive and use machines

Patients who experience dizziness, vertigo, somnolence or other central nervous system disturbances, including visual disturbances, while taking NSAIDs should refrain from driving or using machines.

4.8 Undesirable effects

Adverse drug reactions from clinical trials and/or spontaneous or literature cases (Table 1) are listed by MedRA system order class. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness. In addition, the corresponding frequency category for each adverse drug reaction is based on using the following convention: (CIOMS III): very common (>1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1,000, < 1/100); rare (≥ 1/10,000, < 1/1,000);

Blood and lymphatic system disorders	
Very rare	Thrombocytopenia, leucopoenia, anaemia (including haemolytic and aplastic anaemia), agranulocytosis.
Immune system disorders	
Rare	Hypersensitivity, anaphylactic and anaphylactoid reactions (including hypotension and shock).
Very rare	Angioneurotic oedema (including face oedema).
Psychiatric disorders	
Very rare	Disorientation, depression, insomnia, nightmare, irritability, psychotic disorder.
Nervous system disorders	
Common	Headache, dizziness.
Rare	Somnolence, tiredness.
Very rare	Paraesthesia, memory impairment, convulsion, anxiety, tremor, aseptic meningitis, taste disturbances, cerebrovascular accident.
Unknown	Confusion, hallucinations, disturbances of sensation, malaise.
Eye disorders	
Very rare	Visual disturbance, vision blurred diplopia.
Unknown	Optic neuritis.
Ear and labyrinth disorders	
Common	Vertigo.
Very rare	Tinnitus, hearing impaired.
Cardiac disorders	
Uncommon*	Myocardial infarction, cardiac failure, palpitations, chest pain.
Not known	Kounis syndrome.

Vascular disorders	
Very rare	Hypertension, hypotension, vasculitis.
Respiratory, thoracic and mediastinal disorders	
Rare	Asthma (including dyspnoea).
Very rare	Pneumonitis.
Gastrointestinal disorders	
Common	Nausea, vomiting, diarrhoea, dyspepsia, abdominal pain, flatulence, anorexia.
Rare	Gastritis, gastrointestinal haemorrhage, haematemesis, diarrhoea haemorrhagic, melaena, gastrointestinal ulcer with or without bleeding or perforation (sometimes fatal particularly in the elderly).
Very rare	Colitis (including haemorrhagic colitis and exacerbation of ulcerative colitis or Crohn's disease), constipation, stomatitis (including ulcerative stomatitis), glossitis, oesophageal disorder, diaphragm-like intestinal strictures, pancreatitis.
Unknown	Ischaemic colitis.
Hepatobiliary disorders	
Common	Transaminases increased.
Rare	Hepatitis, jaundice, liver disorder.
Very rare	Fulminant hepatitis, hepatic necrosis, hepatic failure.
Skin and subcutaneous tissue disorders	
Common	Rash.
Rare	Urticaria.
Very rare	Bullous eruptions, eczema, erythema, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell's syndrome), dermatitis exfoliative, loss of hair, photosensitivity reaction, purpura, allergic purpura, pruritus.
Not Known	Fixed drug eruption, generalised bullous fixed drug eruption.

Renal and urinary disorders	
Very rare	Acute renal failure, haematuria, proteinuria, nephrotic syndrome, interstitial nephritis, renal papillary necrosis.
Reproductive system and breast disorders	
Very rare	Impotence.
General disorders and administration site conditions	
Rare	Oedema.

Reporting of suspected adverse reactions:
Reporting suspected adverse reactions after authorisation of the medicinal product is important as it allows continued monitoring of the benefit–risk balance of the medicinal product. Healthcare professionals are requested to report any suspected adverse reactions to the marketing authorisation holder or, where applicable, via the national reporting system.

4.9 Overdose

Symptoms There is no typical clinical picture resulting from diclofenac overdosage. Overdosage can cause symptoms such as vomiting, gastrointestinal haemorrhage, diarrhoea, dizziness, tinnitus or convulsions. In the event of significant poisoning, acute renal failure and liver damage are possible. Therapeutic measures Management of acute poisoning with NSAIDs, including diclofenac, essentially consists of supportive measures and symptomatic treatment. Supportive measures and symptomatic treatment should be given for complications such as hypotension, renal failure, convulsions, gastrointestinal disorder, and respiratory depression.

5.PHARMACOLOGICAL PARTICULARS

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, non-steroids, acetic acid derivatives and related substances (ATC code: M01A B05). Mechanism of action ZOFENAC 50 contains the potassium salt of diclofenac, a non-steroidal compound with pronounced analgesic, anti-inflammatory and antipyretic properties. Inhibition of prostaglandin biosynthesis, which has been demonstrated in experiments, is considered to be fundamental to its mechanism of action. Prostaglandins play a major role in causing inflammation, pain and fever. ZOFENAC 50 tablets have a rapid onset

of action which makes them particularly suitable for the treatment of acute painful and inflammatory conditions. Diclofenac potassium in vitro does not suppress proteoglycan biosynthesis in cartilage at concentrations equivalent to those reached in humans.

ZOFENAC 50 has been found to exert a pronounced analgesic effect in moderate and severe pain. In the presence of inflammation, e.g. due to trauma or following surgical interventions, it rapidly relieves both spontaneous pain and pain on movement and diminishes inflammatory swelling and wound oedema. Clinical studies have also revealed that in primary dysmenorrhoea the active substance is capable of relieving the pain and reducing the extent of bleeding. In migraine attacks ZOFENAC 50 has been shown to be effective in relieving the headache and in improving the accompanying symptoms of nausea and vomiting. There is limited clinical trial experience of the use of diclofenac in Juvenile Rheumatoid Arthritis (JRA)/Juvenile Idiopathic Arthritis (JIA) paediatric patients. In a randomized, double-blind, 2week, parallel group study in children aged 3-15 years with JRA/JIA, the efficacy and safety of daily 2-3 mg/kg BW diclofenac was compared with acetylsalicylic acid (ASS, 50-100 mg/kg BW/d) and placebo – 15 patients in each group. In the global evaluation, 11 of 15 diclofenac patients, 6 of 12 aspirin and 4 of 15 placebo patients showed improvement with the difference being statistically significant ($p < 0.05$). The number of tender joints decreased with diclofenac and ASS but increased with placebo. In a second randomized, double-blind, 6-week, parallel group study in children aged 4-15 years with JRA/JIA, the efficacy of diclofenac (daily dose 2-3 mg/kg BW, n=22) was comparable with that of indomethacin (daily dose 2-3mg/kg BW, n=23).

5.2 Pharmacokinetic properties

Absorption: Diclofenac is rapidly and completely absorbed from diclofenac potassium tablets. The absorption sets in immediately after administration and the same amount is absorbed as from an equivalent dose of diclofenac sodium gastro-resistant tablets. Mean peak plasma concentrations of 3.8micromol/L are attained after 20 - 60 minutes after ingestion of one tablet of 50mg. Ingestion together with food has no influence on the amount of diclofenac absorbed although onset and rate of absorption may be slightly delayed. Since about half of diclofenac is metabolized during its first passage through the liver (first pass effect), the area under the concentration curve (AUC) is about half as large following oral or rectal administration as it is following a parenteral dose of equal size. The amount absorbed is in linear proportion to the size of the dose.

Pharmacokinetic behaviour does not change after repeated administration. No accumulation occurs provided the recommended dosage intervals are observed.

Distribution: The active substance is 99.7% protein bound, mainly to albumin (99.4%). Diclofenac enters the synovial fluid, where maximum concentrations are measured 2-4 hours after peak plasma values have been attained. The apparent half-life for elimination from the synovial fluid is 3-6 hours. Two hours after reaching the peak plasma values, concentrations of the active substance are already higher in the synovial fluid than they are in the plasma, and remain higher for up to 12 hours.

Diclofenac was detected in a low concentration (100 ng/mL) in breast milk in one nursing mother. The estimated amount ingested by an infant consuming breast milk is equivalent to a 0.03 mg/kg/day dose.

Biotransformation/Metabolism: Biotransformation of diclofenac takes place partly by glucuronidation of the intact molecule, but mainly by single and multiple hydroxylation and methoxylation, resulting in several phenolic metabolites, most of which are converted to glucuronide conjugates. wo phenolic metabolites are biologically active, but to a much lesser extent than diclofenac.

Elimination: Total systemic clearance of diclofenac in plasma is 263 ± 56mL/min (mean value SD). The terminal half-life in plasma is 1-2 hours. Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours.

5.3 Pre-clinical Safety

Not applicable

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients:

Maize Starch
Micro crystalline cellulose
Polyvinyl Pyrrolidone (P.V.P. K-30)
Isopropyl Alcohol
Purified Talc
Magnesium Stearate
Sodium Starch Glycolate
Colloidal Anhydrous Silica
HPMC 15CPS
Methylene Chloride
Talcum
PEG 6000
Tween -80

Colour : Yellow Iron Oxide

6.2 Incompatibilities:
Nil.

6.3 Shelf Life:
36 months.

6.4 Special Precautions for storage:
Store in dry place below 30^0C. Protect from light.

6.5 Nature and contents of container:
BLISTER PACK

6.6 Special precautions for disposal and other handling
No special requirements.

7. MANUFACTURING AUTHORIZATION HOLDER AND MANUFACTURING SITE ADDRESS
ZAIN PHARMA LIMITED
Plot No: 209/13741, Colchester Park,
Go-Down No.1, 2, 3, Off Mombasa Road,
Behind Nice and Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya

8. MARKETING AUTHORIZATION NUMBER
H2025/CTD11719/24990

9. DATE OF FIRST AUTHORIZATION /RENEWAL OF THE AUTHORIZATION
06/12/2025

10. DATE OF REVISION OF TEXT
06/12/2025